#3
11/1/02

222.94213.CON2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner: Samuel A. BARTS Art Unit: 1621

In re: Application of: Ronald B. MILLER, et al.

Serial No.: 09/800,204

Filed: March 6, 2001

For: **CONTROLLED RELEASE TRAMADOL**

RESPONSE UNDER 37 C.F.R. § 1.111

Assistant Commissioner for Patents
Washington, D.C. 20231

October 23, 2002

Sirs:

In response to the Office Action mailed April 23, 2002, Applicants respectfully submit the following remarks:

REJECTION UNDER 35 U.S.C. § 103(a):

In the Office Action, the Examiner rejected claims 1-19 and 21-41 under 35 U.S.C. § 103(a) as being unpatentable over Raffa *et al.* ((Caplus 1992:120745, J. Pharmacol. Exp. Ther. 1992, 260 (1), 275-85)) in view of EP 0147780 to Bondi ("the Bondi patent"). The Examiner stated that "Raffa et al teach the use of Tramadol hydrochloride as a pain medicament with opioid and nonopioid properties... The instant claimed invention differs from the prior art by requiring a controlled release composition... The secondary reference to Bondi teaches a controlled release method for a variety of compounds of which Tramadol is listed as an example... It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the controlled release method taught in Bondi for making an oral composition of Tramadol... The claims drawn to specific amounts, specific dosage forms,

specific dissolution rates etc., are all obvious since a skilled artisan would reasonably be expected to tweak the controlled release form of Tramadol [of Bondi] to meet a variety of needs"

These rejections are respectfully traversed. At the very least, it is respectfully submitted that the Raffa reference and the Bondi patent are not properly combinable. According to the abstract of the Raffa reference, tramadol was administered to rats by intracerebral-ventricular and intrathecal administration. The Raffa reference does not contemplate controlled release oral dosage forms. In contrast, the Bondi reference purports to describe controlled release drug delivery systems of a plethora of active agents and does not contemplate immediate release dosage forms. Accordingly, one skilled in the art would not be motivated to combine the Raffa reference with the Bondi reference.

Further, the Bondi reference includes tramadol in an exhaustive list of possible active agents which can be included in the drug delivery device described therein. Due to the large scope of listed compounds in this reference, one skilled in the art would not view this reference as teaching tramadol controlled release formulations. Accordingly, one skilled in the art would not combine the Bondi reference with the Raffa reference which is specifically directed to tramadol.

Even assuming arguendo that these references were properly combinable, it is respectfully submitted that one skilled in the art would not arrive at the present invention based on the combination of the cited references. The Examiner is directed to independent claims 1 and 31 which are as follows:

1. *A solid controlled release oral dosage form, comprising a therapeutically effective amount of tramadol or a pharmaceutically acceptable salt thereof incorporated into a matrix such that said dosage form <u>provides a therapeutic effect for at least about 24 hours</u>. (Emphasis added)*

31. *A solid controlled release oral dosage form, comprising a therapeutically effective amount of tramadol or a pharmaceutically acceptable salt thereof incorporated into a matrix such that said dosage form provides a therapeutic effect for at least about 12 hours. (Emphasis added)*

As recited in the present claims, the present invention is directed to oral dosage forms comprising tramadol which provide specific pharmacokinetic parameters, i.e., a therapeutic effect for at least about 12 hours or 24 hours. The Bondi reference merely states that the drug delivery devices described therein are useful for "dispensing a composition of matter at a controlled rate for a prolonged period of time." The Bondi reference does not teach that the formulations described therein provide a therapeutic effect for at least about 12 hours or 24 hours as recited in the present claims. Furthermore, the Bondi reference does not suggest that the formulations described therein can be modified to attain the claimed pharmacokinetic parameters. Accordingly, one skilled in the art would not arrive at the present invention based on a combination of the Raffa and Bondi references.

CONCLUSION

Claims 1 and 21-41 are pending. In view of the arguments made, Applicants respectfully submit that the pending claims are in condition for allowance. An early and favorable action on the merits is earnestly solicited.

A check in the amount of $920.00 is enclosed for the fee for a three-month extension of time. If it is determined that any additional fees are due or that any fees have been overpaid, the Commissioner for Patents is hereby authorized to charge said fees or credit any overpayment to Deposit Account No. 50-0552.

In addition, Applicants submit herewith a Supplemental Information Disclosure Statement and Attachments A-D. Attachments A-D were previously submitted during the prosecution of the parent case, U.S. Serial No, 08/449,772, now U.S. Patent No. 6,326,027.

Respectfully submitted,

DAVIDSON, DAVIDSON & KAPPEL, LLC

By: _____

Robert J. Paradiso
Reg. No. 41, 240

Davidson, Davidson & Kappel, LLC
485 Seventh Avenue, 14th Floor
New York, New York 10018
(212) 736-1940